88. (New) An isolated nucleic acid comprising a nucleic acid sequence that encodes a polypeptide of SEQ ID NO: 4.

89. (New) An isolated nucleic acid comprising a nucleic acid sequence that encodes a polypeptide selected from the group consisting of residues 4-22, 140-148, 205-218, 68-90, 191-201, 274-289, 110-133, 51-62, 226-241, 151-163, 168-181, 297-302, 27-34, and 97-107 of SEQ ID NO: 4.

90. (New) A vector comprising the nucleic acid sequence of any one of claims 61-72 and 77-89.

91. (New) A host cell comprising the vector of claim 90.

REMARKS

Claims 61-76 are pending in the application. Following entry of the above amendment, claims 61-91 are pending. Claims 61-76 have been amended and claims 77-91 have been added. Applicants submit that the amendment does not introduce new matter and that it is made without any intention to abandon the subject matter as filed, and with the intention that claims of the same, greater, or lesser scope may be filed in a continuing application.

Claims 64, 66, and 74-76 were amended to correct punctuation. Claim 68 was amended to delete "encoding a functional fragment having specific HS binding affinity." Claims 69-73 were amended to correct dependency. Support for the amendments to claims 61-63, 65, and 67-76, as well as for new claims 77-91, may be found, for example, on the following pages within Applicants' Specification:

Claim	Support in the Specification	Claim	Support in the Specification
61	Page 3, lines 22-29; Page 8, line 5-20; Page 11, line 27 to Page 12, line 12; Page 13, lines 7-9;	83	Page 13, lines 6-7.

Claim	Support in the Specification	Claim	Support in the Specification
	Page 18, line 6 to Page 20, line 6.		
62	Page 3, lines 22-23; Page 4, line 6.	84	Page 3, lines 22-29; Page 4, line 7; Page 18, lines 6-29.
63	Page 3, lines 22-23; Page 4, line 7.	85	Page 13, lines 7-9; Page 18, line 29 to Page 19, line 4.
65	Page 13, lines 7-9; Page 18, line 29 to Page 19, line 4.	86	Page 13, lines 7-9; Page 18, line 30 to Page 19, line 4.
67	Page 4, line 6-7.	87	Page 18, lines 6-29.
77	Page 13, lines 7-9; Page 18, line 30 to Page 19, line 4.	88	Page 18, lines 6-29.
78	Page 18, lines 6-29.	89	Page 18, lines 6-29; Page 29, lines 1-3.
79	Page 18, lines 6-29.	90	Page 19, lines 10-18.
80	Page 4, lines 6-7; Page 13, line 24; Page 18, lines 6-29.	91	Page 20, lines 28-32.
81	Page 18, lines 6-29; Page 29, line 1.		
82	Page 3, lines 22-29; Page 8, line 5-20; Page 11, line 27 to Page 12, line 12; Page 13, lines 7-9; Page 18, line 6 to Page 20, line 6.		

Oath/Declaration

Applicants submit herewith a substitute Combined Declaration and Power of Attorney form for each inventor.

Rejection of Claims Under 35 U.S.C. §112, first paragraph

On page 4 of the Office Action, the Examiner rejects claims 61-63 under 35 U.S.C. §112, first paragraph, for lack of enablement, contending that these claims encompass any allelic variant such that an "artisan of skill would have required extensive experimentation to practice the claimed invention commensurate with the scope of the claims". Applicants traverse the rejection to the extent it is maintained over the claims as amended.

The enablement standard requires that the specification provide a description that, when coupled with knowledge possessed by a person of ordinary skill in the art, enables that person to make and use the claimed invention. Atlas Powder Co. v. E. I. Dupont De Nemours & Co., 750 F. 2d 1569, 1576 (Fed. Cir. 1984). Enablement is not precluded by the necessity for some experimentation; however, any required experimentation must not be undue experimentation. In re Wands, 858 F.2d 731, 736-7 (Fed. Cir. 1988). The key word is "undue, " not "experimentation". In re Angstadt, 537 F.2d 489, 504 (C.C.P.A. 1976).

Applicants submit that for the reasons below the amended and new claims are enabled. Applicants have disclosed the isolated nucleic acid sequences that encode mouse and human 3-OST-1 proteins (nucleotide sequences SEQ ID NOS: 1 and 3, respectively, which correspond to protein sequences SEQ ID NOS: 2 and 4, respectively). The disclosure of these sequences allows one skilled in the art to identify variant nucleic acid sequences, and homologues in other species, by standard techniques without undue experimentation. Furthermore, Applicants have taught various assays whereby polypeptides encoded by variant nucleic acids can be tested for 3-0-sulfotransferase activity (Applicants' Specification, page 47, lines 12-18, for example). Applicants also disclose assays for identifying the 3-0-sulfotransferase reaction products and the site of sulfation on heparan sulfate (Applicants' Specification, page 47, line 20 to page 48, line 17 and page 52, line 19 to page 54, line 8, for example). The methods described are performed readily by one skilled in the art and involve contacting a polysaccharide with a 3-0-sulfotransferase polypeptide variant in the presence of a sulfate donor and determining if the variant 3-0-sulfotransferase polypeptide 3-0-sulfates the polysaccharide (e.g., converts the GlcA→GlcNS ±6S to GlcA→GlcNS 3S±6S). Furthermore, the activity of variant polypeptides

may be tested by determining if they can enrich the AT-binding fraction of a heparan sulfate pool, as described on page 35, lines 7-28 of Applicants' Specification. Given the abundance of guidance in Applicants' Specification for determining whether a polypeptide encoded by the nucleic acids will encode proteins that retain 3-0-sulfating activity, Applicants submit that a skilled artisan would readily, and without undue experimentation, be able to make and identify variant 3-OST-1 proteins encompassed by the present claims.

Applicants respectfully request that the rejections under 35 U.S.C. §112, first paragraph, be reconsidered and withdrawn.

Rejection of Claims Under 35 U.S.C. §112, second paragraph

On page 4 of the Office Action, the Examiner rejects claims 68 and 73 under 35 U.S.C. §112, first paragraph for indefiniteness.

Claim 68 has been amended to remove reference to a functional fragment, thereby rendering the rejection of claim 68 and dependent claim 73 moot.

Applicants respectfully request that the rejections under 35 U.S.C. §112, second paragraph be reconsidered and withdrawn.

Rejection of Claims Under 35 U.S.C. §102

On page 5 of the Office Action, the Examiner rejects claims 61, 73, and 74 under 35 U.S.C. §102(a) as being anticipated by Marra et al. (EST database accession no. AA041885) (hereinafter referred to as "Marra I"). The Examiner contends that Marra I discloses a nucleic acid identical to the sequence that encodes 246-272 of SEQ ID NO: 4. Applicants traverse the rejection to the extent it is maintained over the claims as amended.

Applicants submit that the claims as amended do not read on Marra I. Marra I discloses an EST sequence encompassing a short stretch of 81 nucleotides. In contrast, amended claim 61 is directed to a nucleic acid sequence comprising nucleotides 323 to 1255 of SEQ ID NO:1, or substitutions or variants thereof, wherein the nucleic acid substitutions or variants encode a

polypeptide having a 3-O-sulfotransferase activity. Although the fragment disclosed in Marra I shares some identity with a portion of SEQ ID NO:1, that fragment does not identically disclose nucleotides 323 to 1255 of SEQ ID NO:1 and does not encode a polypeptide having 3-0-sulfotransferase activity. In addition, the new independent claims recite either longer, active polypeptides (claims 78-80, 82, 84, 85, 87, and 88) or different fragments (claims 81 and 89). Applicants thus respectfully submit that the nucleic acid sequence of Marra I falls outside the scope of the claims as amended.

On page 5 of the Office Action, the Examiner rejects claims 61, 68, 73, and 74 under 35 U.S.C. §102(a) as being anticipated by Marra et al. (EST database accession no. W62484) (hereinafter referred to as "Marra II"). The Examiner contends that Marra II discloses a nucleic acid identical to the sequence that encodes 250-276 of SEQ ID NO: 2. Applicants traverse the rejection to the extent it is maintained over the claims as amended.

Applicants submit that the claims as amended do not read on Marra II. Marra II discloses an EST sequence encompassing a short stretch of 81 nucleotides. In contrast, amended claim 61 is directed to a nucleic acid sequence comprising nucleotides 323 to 1255 of SEQ ID NO:1, or substitutions or variants thereof, wherein the nucleic acid substitutions or variants encode a polypeptide having a 3-O-sulfotransferase activity. Although the fragment disclosed in Marra II shares some sequence identity with a portion of SEQ ID NO:1, that fragment does not encode a polypeptide having 3-0-sulfotransferase activity. In addition, the new independent claims recite either longer, active polypeptides (claims 78-80, 82, 84, 85, 87, and 88) or different fragments (claims 81 and 89). Applicants thus respectfully submit that the nucleic acid sequence of Marra II falls outside the scope of the claims as amended.

Applicants respectfully request the rejections under 35 U.S.C. §102(b) be reconsidered and withdrawn.

CONCLUSION

Applicants submit that all claims as amended are allowable and respectfully request early and favorable action by the Examiner. If the Examiner believes that a telephonic interview with

Applicants' agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned.

Respectfully submitted,

Dated: December 30, 2002

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MARKED-UP COPY OF AMENDED CLAIMS

61. (Amended) An isolated nucleic acid [encoding a 3-OST protein, wherein the nucleic acid encodes a 3-O-sulfotransferase domain of a 3-OST-1 protein] sequence comprising nucleotides 323 to 1255 of SEQ ID NO:1, or substitutions or variants thereof, wherein the nucleic acid substitutions or variants encode a polypeptide having 3-O-sulfotransferase activity.

62. (Amended) The isolated nucleic acid of claim [61]82, wherein the nucleic acid encodes [a 3-OST protein comprising] a mature human 3-OST-1 protein comprising residues 21-307 of SEQ ID NO: 4.

63. (Amended) The isolated nucleic acid of claim 61, wherein the nucleic acid encodes [a 3-OST protein comprising] a mature murine 3-OST-1 protein comprising residues 21-311 of SEQ ID NO: 2.

64. (Amended) The isolated nucleic acid of claim 61, wherein the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 1.

65. (Amended) [The] An isolated nucleic acid [of claim 61 wherein the nucleic acid comprises a] sequence having at least [85%] 70% nucleotide sequence identity with nucleotides 323 to 1255 of SEQ ID NO:1, wherein the nucleic acid sequence encodes a polypeptide having 3-O-sulfotransferase activity [and encodes a functional fragment having sequence-specific HS binding affinity].

66. (Amended) The isolated nucleic acid of claim 61, wherein the nucleic acid comprises a nucleotide sequence encoding residues 21-307 of SEQ ID NO: 2.

67. (Amended) The isolated nucleic acid of claim 61, wherein the nucleic acid comprises a nucleotide sequence encoding residues 53-311, 21-52, or 260-269 of SEQ ID NO: 2.

68. (Amended) The isolated nucleic acid of claim 61, wherein the nucleic acid comprises a nucleotide sequence encoding residues 250-276 of SEQ ID NO: 2 [encoding a functional fragment having specific HS binding affinity].

69. (Amended) The isolated nucleic acid of claim [61] 82, wherein the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 3.

70. (Amended) The isolated nucleic acid of claim [61] 82, wherein the nucleic acid comprises a nucleotide sequence encoding residues 21-303 of SEQ ID NO: 4.

71. (Amended) The isolated nucleic acid of claim [61] 82, wherein the nucleic acid comprises a nucleotide sequence encoding residues 49-307 of SEQ ID NO: 4.

72. (Amended) The isolated nucleic acid of claim [61] 82, wherein the nucleic acid comprises a nucleotide sequence encoding residues 246-272 of SEQ ID NO: 4 [and encoding a functional fragment having specific HS binding affinity].

73. (Amended) A host cell transformed with a nucleic acid of any one of claims 61-72 and 77-89, or a descendant thereof.

74. (Amended) The host cell of claim 73, wherein the host cell is selected from the group consisting of bacterial cells, yeast cells, and insect cells.

75. (Amended) The host cell of claim 73, wherein the cell is a mammalian cell.

76. (Amended) The host cell of claim 73, wherein the cell is selected from the group consisting of COS-7 cells, CHO cells, murine primary cardiac microvascular endothelial cells (CME), murine mast cell line C57.1, human primary endothelial cells of umbilical vein (HUVEC), F9 embryonal carcinoma cells, rat fat pad endothelial cells (RFPEC), and L cells.

77. (New) The isolated nucleic acid of claim 65, wherein the nucleic acid sequence has at least 85% nucleotide sequence identity with nucleotides 323 to 1255 of SEQ ID NO: 1.

78. (New) An isolated nucleic acid comprising a nucleic acid sequence that encodes a polypeptide of SEQ ID NO: 2, or polypeptide variant thereof, wherein the polypeptide variant has 3-O-sulfotransferase activity.

79. (New) An isolated nucleic acid comprising a nucleic acid sequence that encodes a polypeptide of SEQ ID NO: 2.

80. (New) An isolated nucleic acid sequence comprising a nucleic acid sequence that encodes residues 53-311 of SEQ ID NO: 2, or polypeptide variant thereof, wherein the polypeptide variant has 3-O-sulfotransferase activity.

81. (New) An isolated nucleic acid comprising a nucleic acid sequence that encodes a polypeptide selected from the group consisting of residues 4-29, 144-152, 208-222, 31-42, 155-181, 72-94, 195-205, 278-293, 113-136, 56-66, 230-245, 301-306, and 101-107 of SEQ ID NO: 2.

82. (New) An isolated nucleic acid comprising nucleotides 119 to 1039 of SEQ ID NO:3, or substitutions or variants thereof, wherein the nucleic acid sequence substitutions or variants encode a polypeptide having 3-O-sulfotransferase activity.

83. (New) The isolated nucleic acid of claim 82, wherein the nucleic acid comprises the nucleotide sequence of SEQ ID NO: 3.

84. (New) An isolated nucleic acid sequence comprising a nucleic acid sequence that encodes residues 49-307 of SEQ ID NO: 4, or polypeptide variant thereof, wherein the polypeptide variant has 3-O-sulfotransferase activity.

85. (New) An isolated nucleic acid sequence having at least 70% nucleotide sequence identity with nucleotides 119 to 1039 of SEQ ID NO: 3, wherein the nucleic acid sequence encodes a polypeptide having 3-O-sulfotransferase activity.

86. (New) The isolated nucleic acid of claim 85, wherein the nucleic acid sequence has at least 85% nucleotide sequence identity with nucleotides 119 to 1039 of SEQ ID NO: 3.

87. (New) An isolated nucleic acid comprising a nucleic acid sequence that encodes a polypeptide of SEQ ID NO: 4, or polypeptide variant thereof, wherein the polypeptide variant has 3-O-sulfotransferase activity.

88. (New) An isolated nucleic acid comprising a nucleic acid sequence that encodes a polypeptide of SEQ ID NO: 4.

89. (New) An isolated nucleic acid comprising a nucleic acid sequence that encodes a polypeptide selected from the group consisting of residues 4-22, 140-148, 205-218, 68-90, 191-201, 274-289, 110-133, 51-62, 226-241, 151-163, 168-181, 297-302, 27-34, and 97-107 of SEQ ID NO: 4.

90. (New) A vector comprising the nucleic acid sequence of any one of claims 61-72 and 77-89.

91. (New) A host cell comprising the vector of claim 90.